

Alerts, Notices, and Case Reports

Cognitive Decline With Nortriptyline Use in a Patient With Dementia of the Alzheimer's Type

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ALONG WITH profound memory and cognitive impairment, patients with dementia of the Alzheimer's type frequently have personality changes, anxiety, depression, and agitation.¹ About 20% to 40% of patients with this dementia have symptoms of moderate to severe depression.¹⁻³ Depression may be more common early in the course of this condition.⁴ Tricyclic antidepressants (TCAs) are frequently prescribed for patients with Alzheimer's-type dementia who have symptoms that suggest a depressive reaction. We report the case of a patient with probable dementia of the Alzheimer's type treated with nortriptyline hydrochloride for a depressive reaction. Nortriptyline therapy was associated with adverse effects resulting in impaired attention, concentration, short-term memory, attention to detail, and visual-spatial tracking.

Report of a Case

The patient, an active 71-year-old married, retired Air Force officer diagnosed with probable dementia of the Alzheimer's type four years earlier, sought admission to an investigational drug trial for this disorder. He was in good health with a previous history of resolved dermatitis and coronary artery bypass grafting in 1983. On initial presentation, he was taking nortriptyline hydrochloride, 75 mg, before bedtime, sublingual nitroglycerin, 0.4 mg (one tablet every other month), and one aspirin daily. He was taking no other prescription or nonprescription medications. Nortriptyline had been prescribed six months earlier for anxiety and sadness over the recent death of a sibling and his own cognitive losses. There were no changes in appetite, sleep, fatigue, restlessness, or suicidal ideation at the time nortriptyline was prescribed.

Admission criteria for the drug trial precluded the use of psychotropic medications. With his regular physician's consent, the nortriptyline dosage was tapered and the drug completely discontinued for a 30-day drug-free period. No serum nortriptyline concentrations were available. When the patient returned for further screening, his wife spontaneously described an increase in alertness, attention, and social in-

volvement without nortriptyline, although he was more easily angered.

His medical records documented two previous administrations of neuropsychological testing. The Wechsler Adult Intelligence Scale-Revised (WAIS-R) and Trailmaking A and B were completed before the patient began nortriptyline therapy and again after six months of taking the drug. Because there had been precipitous cognitive decline on the second administration, the tests were repeated to determine whether cognitive function had declined, remained the same, or improved. The patient's score on a Mini-Mental State (MMS)⁵ evaluation was 16 of 30 while receiving nortriptyline for six months. His MMS score improved slightly to 18 of 30 after the 30-day drug-free period. This was not clinically significant.

Figure 1 shows the results of the three administrations of the selected neuropsychological tests. Overall, the patient's performance declined after six months of taking nortriptyline and improved after it was discontinued. Digit Span, a subtest of the WAIS-R, is a measure of short-term auditory memory for number sequences and reflects attention span and ability to concentrate.^{6,7} This patient showed above-average ability before nortriptyline use, below average while taking the drug, and a return to baseline after the drug was discontinued. Nonverbal reasoning, perceptual organization, and ability to process visual material are measured by the Performance IQ subscale.^{7,8} Picture Completion, a subtest of the Performance IQ, measures alertness to visual detail and ability to grasp the meaning of visual details in a larger context.⁵ Abstract problem solving and spatial relations are measured by the Block Design, and Digit Symbol task measures visual-

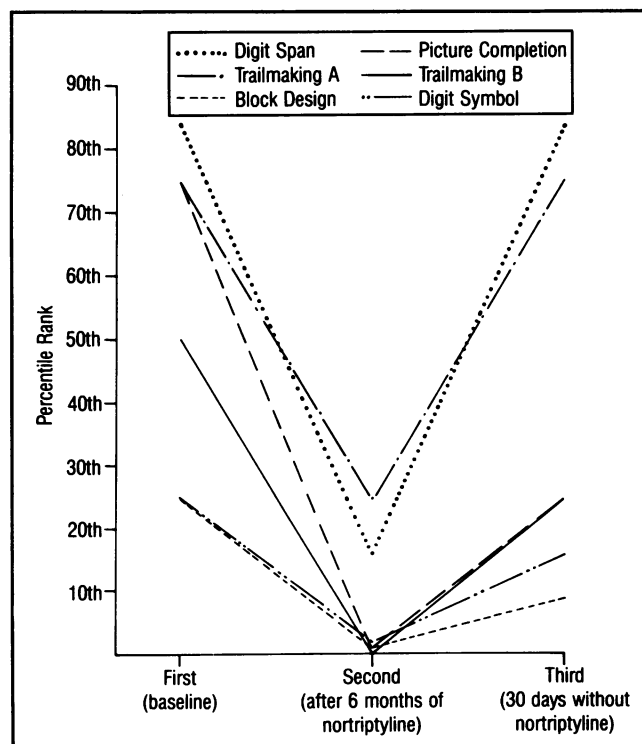


Figure 1.—The diagram shows the patient's performance on select neuropsychological tasks across the three evaluations before, during, and after nortriptyline hydrochloride therapy.

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ABBREVIATIONS USED IN TEXT

MMS = Mini-Mental State
TCA = tricyclic antidepressant
WAIS-R = Wechsler Adult Intelligence Scale-Revised

motor speed.^{6,7} Ability on the Digit Symbol task is enhanced by short-term memory. The overall Performance IQ changed significantly across the three measurement points, suggesting that nonverbal ability declined while the patient was taking nortriptyline and improved subsequent to discontinuation. His performance on Block Design and Digit Symbol showed the same trend, although the change was of lesser magnitude.

Trailmaking A and B are measures of visual-spatial tracking under timed conditions and with increasing task complexity.⁶ A decline in this task is a common finding among patients with dementia of the Alzheimer's type.⁸ The patient's initial performance placed him in the 75th percentile on Trailmaking A and in the 50th percentile on Trailmaking B. While taking nortriptyline, his performance declined to the 10th to 25th percentile for Trailmaking A and he was unable to complete Trailmaking B. After nortriptyline use was terminated, his performance returned to baseline for Trailmaking A and to the 25th percentile for Trailmaking B.

Nortriptyline therapy in this patient resulted in measurable impairment in attention, concentration, short-term memory, attention to detail, and visual-spatial tracking. In addition, the MMS evaluation did not measure those cognitive functions that declined the most while this patient was taking nortriptyline. Although the neuropsychological tests are standardized, three different trained psychologists tested the patient under different conditions. Variations in testing scores could account for some of the differences seen. The direction of the results is consistent across the tests and subtests and congruent with the spouse's anecdotal reports.

Discussion

Tricyclic antidepressant agents may produce decrements in learning and memory in elderly patients.⁹ A complex interaction may occur in patients with dementia of the Alzheimer's type and coexisting depression who receive these drugs. The anticholinergic activity of TCAs is responsible for cognitive impairment, which may either conceal improved cognition due to the alleviation of depression or result in further cognitive impairment due to neurochemical abnormalities associated with Alzheimer's-type dementia. Gross cognitive impairment is uncommon with TCA use at therapeutic serum concentrations.¹⁰ Although subtle and specific disturbances of learning and memory can occur with lower dosages, these deficits may not be recognized. They contribute, however, to the patient's functional impairment unless cognition is evaluated.

Elderly patients are more susceptible than younger patients to the central nervous system anticholinergic effects of TCAs.¹⁰⁻¹² Further, elderly patients with dementia of the Alzheimer's type are more sensitive than age-matched controls to the effects of anticholinergic agents on tests of learning and memory.¹³

Cognitive impairment is related to TCA serum concentrations.^{9,10} In general, elderly patients require a 50% reduction in the dosage of TCAs because of normal physiologic age-related changes that result in reduced metabolism and in-

creased sensitivity to the drugs.^{4,10,11} In this case the patient was maintained on a regimen of 75 mg of nortriptyline daily, a dose more appropriate for a young, healthy adult. Because there were no nortriptyline serum concentrations available, nortriptyline toxicity cannot be ruled out. The dramatic decrease in his cognitive performance may not have occurred on a lower, more appropriate dose.

Few studies have used specific neuropsychological tests to document cognitive impairment in patients treated with TCAs. Most studies commonly rely on the Mini-Mental State evaluation, which may not be specific or sensitive enough to detect cognitive changes, as evidenced by this patient. In a double-blind study using imipramine hydrochloride for depression in patients with Alzheimer's-type dementia, the MMS scores of all subjects improved although activities of daily living and other cognitive measures declined.¹⁴ In another report, administering 50 mg of amitriptyline hydrochloride resulted in impairment on cognitive skills performance tasks such as the vigilance task, the divided attention task, and the critical tracking task.¹⁵ In another study, the use of amitriptyline produced sedation and impaired coordination and cognitive performance such as digit substitution.¹⁶

Additional studies using specific neuropsychological testing are required. The ability to determine cognitive decline in patients with dementia of the Alzheimer's type would be useful in assessing possible benefits versus risks in prescribing psychotropic drugs. Until adequate controlled studies have been completed, some guidelines can be offered. First, patients presenting with symptoms of both depression and dementia require a thorough workup including neuropsychological testing. A limited cognitive assessment using the Dementia Rating Scale⁸ establishes a baseline useful in evaluating change over time and response to treatment. Second, not all patients with Alzheimer's-type dementia who have depressive symptoms meet the criteria for a major affective disorder.¹ This patient was probably experiencing a grief reaction. Similar patients may benefit from psychotherapy rather than medication.¹⁷ Selected patients with Alzheimer's-type dementia become more grief stricken than biologically depressed and may benefit from an opportunity to talk about their losses. Our experience and that of others^{1,17} indicate that these patients are able to establish relationships with professionals. Third, some patients with Alzheimer's-type dementia do experience depression requiring pharmacologic treatment. Elderly patients generally require a 50% reduction in TCA dosage compared with young adults^{10,11} because of changes in clearance, volume of distribution, and the elimination half-life. Elderly patients do achieve normal therapeutic serum concentrations with lower dosages. Patients with Alzheimer's-type dementia may require even lower dosages of the TCAs.¹² Serum concentrations for nortriptyline and imipramine are reliable and useful in evaluating efficacy and response and avoiding unnecessary cognitive impairment or toxicity.

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The Physician as Erotomanic Object

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EROTOMANIA, or De Clérambault's syndrome, attracts attention from several perspectives: nosological, psychological, and biological.¹⁻³ De Clérambault's syndrome borrows its name from the 20th-century French psychiatrist who described "psychose passionnelle"—a condition whose central feature is a delusion in which usually a woman believes that an older man of higher social status is in love with her.^{1,4} The traditional definition of De Clérambault's syndrome as being a predominantly female condition has not been borne out, however.^{5,6} The most recent psychiatric nosology, *Diagnostic and Statistical Manual of Mental Disorders*, third edition, revised (DSM-III-R), has carved out a specific niche for De Clérambault's syndrome as a delusional (paranoid) disorder, erotomanic type.^{1,7}

Perhaps the most vexing dilemma raised by this condition is the forensic one. Erotomanic persons cause significant problems for the misinterpreted object of their delusion. A perusal through newspapers and popular magazines finds many articles reporting the escapades or criminal acts of persons whose erotomanic targets are celebrities and politicians. From a forensic perspective, the two most recently prominent persons possibly suffering from erotomanic delusions have been John Hinckley, Jr, who attempted to assassinate then-President Reagan, and Prosenjit Poddar of the landmark legal case of *Tarasoff v. Regents of University of California*.⁶

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Physicians have not been exempt from becoming the object or target of an erotomanic delusion.⁸⁻¹⁰ We describe the case of a male patient in whom an erotomanic delusion developed involving his female physician. We then explore the possible psychiatric-legal interventions and unresolved issues in these cases.

Report of a Case

The patient, a 39-year-old, never married, Syrian-American man, was involuntarily admitted to hospital for presenting a danger to his 40-year-old married, Syrian-American family physician, his erotomanic object. The patient first encountered the physician seven years ago after he took his mother to the physician's office for monthly visits after a stroke. The physician later became his personal physician as well. About a year before his psychiatric hospital commitment, the delusion developed that there was a romantic relationship between the physician and the patient as a result of his belief that she was secretly falling in love with him. Over the next several months, he made many telephone calls to the physician, sent her a "love letter" by registered mail, and sent her numerous gifts, including an engagement ring. He spent a great deal of time at the hospital where the physician attended patients and at her hair salon. Because the patient did not comply with the physician's requests to leave her alone, she obtained a restraining order to allow for his arrest if he continued to contact her. The patient remained undeterred and made several attempts over the next several months to contact her to complain about the restraining order. He not only telephoned and paged her answering service but continued to visit her office and the hospital. Four months after the restraining order was filed, on Valentine's Day, the patient sent the physician a Valentine's Day card with a letter accusing her of "gross misconduct," "mismanaging his mother's care," and having "played" on his emotions. He signed the letter, "love always." He was arrested about a month later for violating the restraining order. While in jail, he telephoned the physician and demanded to see her alone "to avoid the inevitable."

This patient had no previous psychiatric contact before the onset of his erotomanic delusion. About a year before the development of his delusion, he began to file lawsuits against various insurance and aerospace companies and believed that he was being monitored by overhead helicopters, that his phone was tapped, and that his apartment had been burglarized with his legal papers being the only items stolen. He had traveled to Washington, DC, to report this harassment to government authorities. He was not given an audience, however, because he had failed to make an appointment. The patient had no history of substance abuse or major medical problems. Although he had completed 2½ years of college, for the past few years he had been able to work only part-time in unskilled jobs and had lived with his elderly mother. He denied having auditory hallucinations.

After his arrest, it was decided that involuntary hospitalization on the basis of posing a "demonstrated" danger to others (California Welfare and Institutions Code §§5300 et seq) for a period of 180 days would be preferable to any legal sanction that could be obtained for a first-offense violation of a restraining order. In addition, treatment of the patient's psychosis could be attempted with hospital admission. The petition for this 180-day involuntary commitment was sustained during a jury trial.